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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,261	08/27/2003	Raymond Kim	20144-003100US	6593

20350 7590 09/18/2009

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
09/18/2009	PAPER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAYMOND KIM

Appeal 2009-002842[1]
Application 10/650,261
Technology Center 1600

Decided: September 18, 2009

Before LORA M. GREEN, RICHARD M. LEBOVITZ, FRANCISCO C. PRATS, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an apparatus for detecting immobilized analytes. The Examiner has rejected the claims as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] Zyomyx, Inc. is the real party in interest.

STATEMENT OF THE CASE

Claims 14-25 are pending and on appeal (App. Br. 3).[2] Claim 14, the only independent claim, is representative and reads as follows:

> 14. An apparatus comprising a molecular analyte layer and a film layer wherein:
>
> (i) the molecular analyte layer comprises a molecular analyte immobilized on a molecular analyte solid support, wherein said molecular analyte comprises a molecular ligand binding site; and
>
> (ii) the film layer comprises a molecular ligand zone having a molecular ligand, wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product.

The Examiner cites the following documents as evidence of unpatentability:

Greenquist	US 4,806,312	Feb. 21, 1989
Bergström	US 5,436,161	Jul. 25, 1995

The following rejections are before us for review:

Claims 14-22 and 25 are rejected under 35 U.S.C. § 102(b) as being anticipated by Greenquist (Ans. 3-7).

Claims 23 and 24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Greenquist and Bergström (Ans. 8-10).

ANTICIPATION

ISSUE

The Examiner finds that Greenquist discloses a multi-zone test device having the two distinct layers recited in claim 14 (Ans. 4). Specifically, the

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[2] Appeal Brief dated March 3, 2008.

Examiner finds that Greenquist's device has a "molecular analyte layer [which] comprises a molecular analyte immobilized on a molecular analyte solid support (col. 5, lines 62-65)," and also a "film layer [which] comprises a molecular ligand zone having a molecular ligand (col. 5, lines 57-61), wherein, upon wetting of the molecular ligand zone, the molecular ligand can diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product (col. 10, lines 12-20)" (*id.* at 4-5).

Appellant contends that Greenquist's device does not anticipate claim 14 because "Greenquist does not provide the limitation of *an analyte that is immobilized in one layer and specifically binds a ligand to produce a detectable product*" (App. Br. 7). In particular, Appellant argues, the Examiner erred in finding that the claim terms "analyte" and "ligand" are interchangeable because claim 14 specifically requires the analyte to be immobilized, "whereas a 'ligand' is capable of diffusing within a ligand zone upon wetting. These terms thus cannot simply switch places in the claims" (*id.*).

Appellant acknowledges that Greenquist includes embodiments in which the labeled reagent is incorporated into the device by pre-binding, rather than mixed with the initial analyte-containing sample (*id.* at 8).

Appellant argues, however:

> [R]egardless of how the labeled ligand is supplied, the labeled ligand as well as the analyte being tested (*i.e.*, the analyte from the test solution) are always mobile at the time the two form a detectable complex. The labeled ligand remains bound to the immobilized analyte in the reagent layer does not migrate into the detection layer to produce a detectable signal. The Greenquist device therefore does not teach an analyte that is immobilized in one layer and specifically binds a ligand to produce a detectable product.

(*Id.*)

Moreover, Appellant argues, the claimed immobilized analyte and Greenquist's immobilized analyte "are used for directly opposite purposes. In the present invention, the immobilized analyte acts to form a detectable complex with a labeled ligand; whereas the role of Greenquist's immobilized analyte is to eliminate the potential false signal from excessive unbound labeled ligand" (*id.* at 9). Therefore, Appellant urges, "the layers of Greenquist's device are not equivalent to the layers of the claimed device in this application" (*id.*).

Appellant does not argue the claims subject to this rejection separately. We select claim 14 as being representative of the rejected subject matter. *See* 37 C.F.R. § 41.37(c)(1)(vii).

In view of the positions advanced by Appellant and the Examiner, the issue with respect to this rejection is whether Appellant has shown that the Examiner erred in finding that Greenquist describes a device with two distinct layers that meet the limitations in claim 14.

FINDINGS OF FACT ("FF")

1. Claim 14 recites an apparatus comprising a molecular analyte layer and a film layer. The molecular analyte layer has a molecular analyte immobilized on a solid support. The molecular analyte includes a molecular ligand binding site.

The film layer has a molecular ligand zone that includes a molecular ligand. The molecular ligand, upon wetting of the molecular ligand zone, must be able to diffusibly migrate to the molecular ligand binding site of the molecular analyte to produce a detectable product.

2. The Specification states:

> "Molecular analyte," as used herein means any non-whole cell compound or molecule of interest for which a diagnostic test is desired. A molecular analyte can be, for example, a protein, peptide, carbohydrate, polysaccharide, glycoprotein, hormone, receptor, antigen, antibody, substrate, metabolite, transition state analog, cofactor, inhibitor, drug, dye, nutrient, growth factor, *etc.*, without limitation.

(Spec. 4.)

3. The Specification states:

> As used herein, a "detectable product" is a substance that produces a detectable signal upon binding of the molecular ligand to the molecular ligand binding site of the molecular analyte. Any suitable type of detectable signal and/or detection methodology may be used, including radioactivity, colorimetric, spectrometric, fluorescence, luminescence, electrochemilluminescence [sic], electrochemistry, fluorescence anisotropy, fluorescence polarization, fluorescent quenching, energy quenching, and the like.

(Spec. 17.)

4. Greenquist discloses a "multizone test device for the determination of analyte from a liquid test medium based on interactions among the analyte, a labeled reagent, an immobilized reagent, and an immobilized interactive detection reagent for the labeled reagent" (Greenquist, col. 4, ll. 10-15).

5. Greenquist discloses that the test device "comprises at least one reagent layer and a detection layer, and, as will be described in greater detail hereinafter, can further include a second reagent layer" (*id.* at col. 5, ll. 55-57).

6. Greenquist discloses that the "reagent layer is incorporated with the immobilized reagent which comprises an immobilized form of the analyte

which is not capable of being solubilized or otherwise removed from the reagent layer upon contact with the test medium" (*id.* at col. 5, ll. 58-62).

7. Greenquist discloses that the "detection layer is incorporated with an immobilized form of an interactive detection reagent for the labeled reagent, which interactive detection reagent is similarly not capable of being solubilized or otherwise removed from the detection layer" (*id.* at col. 5, ll. 62- 66).

8. Figure 1 of Greenquist is reproduced below:

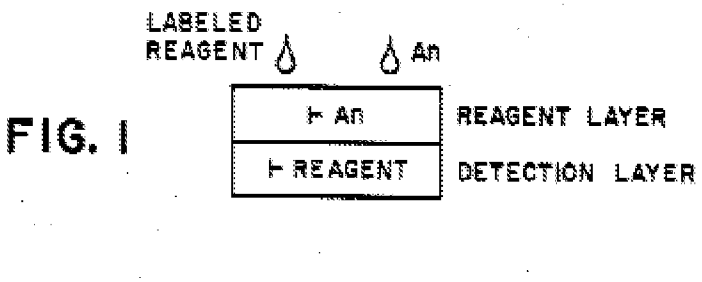

FIG. 1

Figure 1 shows an embodiment of the multilayer test device

> which comprises at least one reagent layer and a detection layer which are in fluid contact with one another. The reagent layer is incorporated with the immobilized form of the analyte (represented as "An"), and the detection layer is incorporated with an immobilized form of an interactive detection reagent for the chemical group label of the labeled reagent (represented as "Reagent") . . . .

(*Id.* at col. 9, ll. 51-58.)

9. Greenquist describes the operation of the device shown in Figure 1 as follows:

> Upon application of both the liquid test medium containing analyte and the labeled reagent to the reagent layer, the test medium and labeled reagent diffuse into the reagent layer and are thereby brought into fluid contact with the

> immobilized analyte in the reagent layer. In this embodiment, the labeled reagent and the test medium can be applied independently or together as a mixture, the latter being preferred since such provides equal competition between the labeled reagent and the analyte from the test medium for binding to the immobilized analyte. Accordingly, any of the analyte present in the liquid test medium becomes bound to the binding partner for the analyte of the labeled reagent and the resulting complex thereby formed is free to migrate within and out of the reagent layer and into the detection layer.

(*Id.* at col. 9, l. 59 through col. 10, l. 6.)

10. Greenquist discloses:

> Alternatively as is known in the art, rather than adding the labeled reagent as a separate component, whether by addition with the liquid test medium or by being incorporated in a separate reagent zone as described in more detail below, the labeled reagent can be prebound to the immobilized reagent in the reagent zone. Since the binding will be reversible, the presence of analyte will reverse some of such binding to release a detectable amount of the labeled reagent.

(*Id.* at col. 10, ll. 12-20.)

11. Greenquist discloses that, in alternative embodiments "[w]here a second reagent layer is employed, the first reagent layer is incorporated with the labeled reagent which is solubilized by the test medium when applied thereto, and the second reagent layer is incorporated with the immobilized form of the analyte" (*id.* at col. 5, l. 66, through col. 7, l. 3).

12. Figure 2 of Greenquist is reproduced below:

FIG. 2

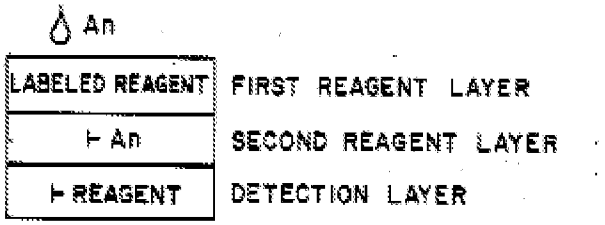

Figure 2 shows a "test device [which] further includes a second reagent layer positioned between the first reagent layer and the detection layer" (*id.* at col. 11, ll. 49-51).

13. Greenquist states that the "additional reagent layer permits incorporation of a test medium soluble form of the labeled reagent therein which obviates the need for pre-mixing the liquid test medium and the labeled reagent prior to the application to the test device or the independent application thereof" (*id.* at col. 11, ll. 51-56).

14. Greenquist describes the operation of the device shown in Figure 2 as follows:

> Upon application of the liquid test medium to the first reagent layer, the liquid test medium diffuses into the first reagent layer bringing any analyte from the test medium into direct fluid contact with the labeled reagent therein while, at the same time, solubilizing the labeled reagent. Accordingly, any analyte from the test medium becomes bound to the binding partner thereof of the labeled reagent and the analyte-(labeled reagent) complex thereby formed migrates within and out of the first reagent layer and into the second reagent layer. It is to be appreciated that any of the unbound labeled reagent in the first reagent layer, i.e., excess labeled reagent, will also migrate within and out of the first reagent layer and into the second reagent layer. Since the binding site of the monovalent binding partner for the analyte of the labeled reagent has been occupied by binding to the analyte from the test medium, once within the second reagent layer, the analyte-(labeled reagent) complex is

> permitted to migrate within and out of the second reagent layer without becoming immobilized, and into the detection layer. Once within the detection layer, the labeled reagent interacts with the immobilized interactive detection reagent incorporated therein to produce the reaction product . . .

(*Id.* at col. 11, l. 67 through col. 12, l. 23.)

15. Greenquist discloses that "since any unbound labeled reagent in the second reagent layer has an available binding site for the immobilized analyte in the second reagent layer, the labeled reagent becomes bound thereto and immobilized thereby and prevented from further migrating into the detection layer" (*id.* at col. 12, ll. 23-28).

16. Regarding suitable detectable moieties Greenquist discloses:

> The labeled reagent of the present invention comprises a binding partner for the analyte under determination, or the analyte or a binding analog thereof, labeled with a chemical group having a detectable chemical or interactive property. It is to be appreciated that the chemical group does not generate a detectable product or otherwise provide a detectable signal prior to interacting with an appropriate interactive detection reagent. Accordingly, the nature of the chemical group of the labeled reagent and the interactive detection reagent necessarily depends upon their interactive properties which generate a reaction product which will provide a detectable signal correlatable to the amount of analyte in a liquid test medium.

(*Id.* at col. 7, ll. 11-24.)

17. Greenquist further discloses:

> [R]epresentative chemical groups possess interactive properties with each other which also permit the use thereof as the interactive detection reagent of the present invention. For example, where the label of the labeled reagent is an enzyme substrate, such as umbelliferone galactose, the immobilized detection reagent is an enzyme capable of hydrolyzing the

> substrate, such as β-galactosidase. Similarly, where the label is an enzyme cofactor, such as nicotinamide adenine dinucleotide, the immobilized detection reagent is an enzyme, such as lactate dehydrogenase. Other representative groups include enzyme prosthetic groups, such as flavin adenine dinucleotide, and an apoenzyme, such as apoglucose oxidase; and enzyme inhibitors, such as methotrexate, and an enzyme which is inhibited by the enzyme inhibitor, such as dihydrofolate reductase. Also, a hapten or other specifically bindable ligand (e.g., biotin) labeled species can be detected with an antibody to the hapten or a protein (e.g., avidin) which binds the ligand tagged or labeled with a detectable molecule. Such detectable molecule can be some molecule with a measurable physical property (e.g., fluorescence or absorbance).

(*Id.* at col. 8, ll. 27-49.)

PRINCIPLES OF LAW

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

During examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

"A patent applicant is free to recite features of an apparatus either structurally or functionally." *Schreiber*, 128 F.3d at 1478. However, "'[f]unctional' terminology may render a claim quite broad . . .[;] a claim employing such language covers *any and all* embodiments which perform

the recited function." *In re Swinehart*, 439 F.2d 210, 213 (CCPA 1971) [emphasis added].

Thus, functional limitations directed to an intended use in an apparatus claim do not serve to distinguish the claimed apparatus from a prior art apparatus inherently capable of performing the claimed function. *See Schreiber*, 128 F.3d at 1478-79 (holding that a prior art apparatus meeting all claimed structural limitations was anticipatory because it was inherently capable of performing the claimed function).

ANALYSIS

Appellant's arguments do not persuade us that the Examiner erred in finding that Greenquist describes a device with two distinct layers that meet the limitations in claim 14.

With respect to the embodiment shown in Figure 1 (*see* FF 8-10), when the labeled reagent is pre-bound to the reagent layer and the analyte-containing test solution is applied to the device, the labeled reagent can migrate to the detection layer (*see* FF 10). Thus, the reagent layer in this embodiment meets the requirement in claim 14 that the film layer includes a ligand capable of diffusibly migrating from the ligand zone to the molecular analyte layer upon wetting of the film layer.

The detection layer in the embodiment shown in Figure 1 can include immobilized detection molecules such as enzymes, which are of course proteins, as well as other binding partners, including enzyme cofactors (FF 17). As Appellant's own Specification concedes, a "molecular analyte" can be virtually any biological molecule of interest, including a protein or a cofactor (FF 2). Thus, we agree with the Examiner that Greenquist's

detection layer has an immobilized moiety that meets the criteria of being a molecular analyte.

We acknowledge, as Appellant argues, that the labeled reagent migrates to the detection zone in the form of a labeled reagent-analyte complex (*see* FF 9). However, this fact does not allow claim 14 to avoid Greenquist's disclosure. Claim 14 does not contain any limitation excluding the ligand from being complexed or bound with additional binding partners. Rather, claim 14 only requires the molecular ligand to be capable of migrating to the molecular ligand binding site of the molecular analyte layer. Greenquist meets the requirement in claim 14 because the labeled reagent when bound to the analyte can, and does, migrate to the molecular ligand binding site (FF 9).

It might be true that Greenquist does not use the term "analyte" to describe the immobilized moieties in the detection layer. However, because the detection layer in the embodiment shown in Figure 1 of Greenquist has an immobilized moiety that falls within Appellant's definition of a molecular analyte, and has a separate layer with a molecular ligand that can migrate to the immobilized moiety when the device is wetted with an analyte-containing solution, we are not persuaded that the Examiner erred in finding that Greenquist meets the limitations of claim 14.

We acknowledge, as Appellant argues (App. Br. 9), that in at least one embodiment Greenquist apparently uses an immobilized analyte to reduce the potential false signal from excessive unbound labeled reagent. For example, Greenquist – as pointed out by Appellants (App. Br. 6) – describes a three layered embodiment as shown in Figure 2, Greenquist discloses that labeled reagent which does not bind to soluble analyte in the sample

becomes bound to the immobilized analyte in the second reagent layer (FF 15).

However, we do not agree that the embodiment shown in Greenquist's three layer embodiment as illustrated in Figure 2 fails to meet the limitations of claim 14. Specifically, the second reagent layer is disclosed as containing immobilized "analyte," as required by claim 14 for the molecular analyte layer (*see* FF 14, 15). Also, the first reagent layer is disclosed as having a labeled reagent that is solubilized by applying the liquid test medium to the strip (FF 14), as claim 14 requires for the molecular ligand in its film layer.

Further, once released, the labeled reagent can diffuse and bind to the immobilized analyte (FF 15), as also required by claim 14. We acknowledge that Greenquist does not disclose detecting this bound product, and instead discloses that only the analyte bound to the detection layer is actually detected (FF 16).

However, claim 14 is directed to an apparatus, not a method. Thus, claim 14 does not recite any step of detecting anything. Because the labeled reagent that binds to the immobilized analyte has, as part of its structure, a moiety that is detectable given the proper reagents (*see* FF 16), the immobilized analyte-labeled reagent complex disclosed by Greenquist is in fact detectable, which is all that claim 14 requires.

In sum, Appellant's arguments do not persuade us that the Examiner erred in finding that Greenquist meets all the limitations of claim 14. We therefore affirm the Examiner's rejection of claim 14 as anticipated by Greenquist. Because they were not argued separately, claims 15-22 and 25 fall with claim 14. *See* 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS

Claims 23 and 24 stand rejected under 35 U.S.C. § 103(a) as being obvious in view of Greenquist and Bergström (Ans. 8-10). Claims 23 and 24 read as follows:

> 23. The apparatus of claim 14, wherein said molecular ligand zone comprises a molecular ligand within a hydrogel.
>
> 24. The apparatus of claim 23, wherein said hydrogel comprises acrylamide or agarose.

The Examiner concedes that Greenquist does not meet the limitations of these claims, and cites Bergström to remedy that deficiency (Ans. 8-9). Based on the references' disclosures, the Examiner concludes that an ordinary artisan would have considered it obvious to use a "molecular ligand comprised within hydrogel comprising agarose as taught by Bergstrom et al., [with] the apparatus comprising a molecular analyte layer and a film layer as taught by Greenquist in order to obtain the essential coupling necessary for a sensing surface that enhances protein compatibility and minimizes nonspecific interactions" (*id.* at 9).

In response to the Examiner's prima facie case of obviousness, Appellant argues only that Bergström fails to provide the limitations previously argued as missing from claim 14, and that the combination of the two references therefore cannot render obvious claims 23 and 24, which both depend from claim 14 (App. Br. 10).

For the reasons discussed above with respect to claim 14, we are not persuaded by this argument. We therefore affirm the Examiner's rejection of claims 23 and 24 as being obvious over Greenquist and Bergström.

SUMMARY

We affirm the Examiner's rejection of claims 14-22 and 25 under 35 U.S.C. § 102(b) as being anticipated by Greenquist.

We also affirm the Examiner's rejection of claims 23 and 24 under 35 U.S.C. § 103(a) as being obvious in view of Greenquist and Bergström.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

alw

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